**c.) Remarks**

*Office Action of May 16, 2005*

Claims 1-4, 6, 8-9, 11-15, and 17-22 are pending. The following claim rejection is outstanding:

1) Rejection of claims 1-4, 6, 8-9, 11-15, and 17-22 under 35 USC § 103(a) as being unpatentable over U.S. Patent 4,851,221 to Pak et al ("Pak") in view of "Calcium and Serum Cholesterol", Nutrition Review, vol. 25, no. 10, pp. 298-300, 1967 (hereinafter "Nutrition Review") or Mitchell et al, "The Effect of Oral Calcium on Cholesterol Metabolism", Journal of Atherosclerosis Research, vol. 8, pp. 913-922, 1968. ("hereinafter "Mitchell").

*1. Rejection of Claims 1-4, 6, 8-9, 11-15, and 17-22 under 35 USC § 103(a)*

In the last substantive office action, the examiner rejected claims 1-4, 6, 8-9, 11-15, and 17-22 under 35 USC § 103(a) as being unpatentable over Pak in view of Nutrition Review or Mitchell. The examiner asserts that Pak discloses the administration of a calcium supplemental composition comprising calcium citrate at a dose of 1 g/day (60 meq/day) or 1.5-2.75 g/day to a postmenopausal woman for treating various conditions such as hypoparathyroidism, osteoporosis, bone loss, hyperphosphatemia, and hypertension. The examiner states that Pak discloses a daily administration and that the composition of Pak is prepared from pre-mix preparation with a calcium/citrate molar ratio of 1.25 of citric acid and a calcium compound such as calcium hydroxide. However, the examiner recognizes that the Pak reference 1) does not expressly disclose the employment of a calcium composition in methods of increasing an HDL level in plasma or a ratio of HDL to LDL in a postmenopausal woman, 2) does not expressly disclose measuring the HDL level in said woman, and importantly, **3) does not expressly**

**disclose the administration of the calcium composition for at least about two months.** (see pending office action at page 3). The examiner asserts that Nutrition Review teaches that oral calcium supplements are known to have hypocholesteremic effect in a person or subject with raised serum cholesterol and that cholesterol levels are known to be measured before and at the end of calcium administration. The examiner also asserts that Mitchell teaches that serum cholesterol levels are known to be measured using an Auto Analyzer (a known method) to test the effect of oral calcium on cholesterol metabolism. The examiner concludes that "it would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer the calcium composition to a postmenpausal woman daily or at least two or six months for increasing a high-density lipoprotein (HDL) in plasma or a ratio of HDL to LDL in said postmenopausal woman; and to measure the high-density lipoprotein level in [a] postmenopausal woman [who has been administered] calcium citrate for increasing HDL level." Applicants respectfully traverse the rejection.

Applicants maintain that the combination under § 103(a) used by the examiner to reject the pending claims is improper because either or both of Mitchell and Nutrition Review teach away from Pak. With respect to Nutrition Review, the abstract of that reference teaches "[t]here is no evidence that this effect is maintained for longer than three or four weeks, and <u>there seems to be no justification for using oral calcium as a means of reducing serum cholesterol levels</u>." (emphasis added). In this way, Nutrition Review clearly teaches away from administration of oral calcium for longer than three or four weeks. With respect to Mitchell, the abstract of that reference teaches: "[t]he serum cholesterol and triglyceride levels showed little change from the basal levels during the calcium supplementation period." Thus, Mitchell also teaches away from the claimed invention.

The examiner relies on MPEP 2123 (and Federal Circuit cases cited therein), asserting that despite any "teaching away", a reference can still anticipate a claim. Applicants assert that MPEP 2123 and the cases cited therein are not applicable to the pending rejection. The MPEP provision cited by the examiner merely stands for the rather unremarkable propositions that 1) a patent reference is prior art for all it discloses and that 2) any of the disclosed embodiments in a patent reference (not solely the preferred embodiment) can render a claim unpatentable. MPEP 2123 clearly addresses only the case of rejections over a single reference (i.e., rejections based upon anticipation under § 102). The cases cited therein only state that the issue of "teaching away" is not relevant to an anticipation analysis (i.e., a patentability analysis under § 102). They stand for the proposition that if a single reference discloses an invention, it is anticipated under § 102, regardless of whether or not the reference also disparages the invention or treats it as a less-than-preferred embodiment. In other words, one part of a reference cannot be said to "teach away" from another part **of the same reference**. (*See Celeritas Technol., Ltd. v. Rockwell Int'l.*, 150 F.3d 1354, 1361 (Fed. Cir. 1998); this case is referenced in MPEP 2123). This is not the case for the pending rejection. The pending rejection is one under § 103(a) for obviousness. In this case, a "teaching away" analysis is very relevant to a rejection over a combination of references **where the teaching of one reference teaches away from the teaching of the other reference**.

The examiner's argument based on MPEP 2123 is further inapposite because that provision merely states that less than optimal embodiments are proper for anticipation and can be used to properly deny patentability so long as they are disclosed. This is inapposite to the pending rejection even if it is possible to extend MPEP 2123 to the context of obviousness under § 103(a) (although such an extension is not proper under the plain language of that provision)

because the secondary references of Nutrition Review and Mitchell do not teach that a 2-month (or longer) therapy is "less than optimal"; rather they teach that such therapy **is not useful**. Thus, even if MPEP 2123 is assumed to be applicable to a § 103(a) analysis (which it is not), the facts of the present case are very different than the scenario addressed in MPEP 2123 and provide a much more compelling basis for patentability.

The applicants discussed the substantive differences between the cited prior art and the pending claims with the examiner in a telephone interview of July 25, 2005. Agreement with regard to the outstanding rejection under § 103(a) was not reached but the examiner noted that submission of data showing unexpected results may be persuasive. To this end, along with a request for continued examination, applicants herein submit a Rule 132 declaration with additional data supporting the patentability of the pending claims.

To further support their assertion that the instant claims are patentable over the references (either alone or in combination) cited by the examiner, applicants submit a Rule 132 declaration of inventor Dr. Ian Reid, along with data which demonstrates that a significant benefit with respect to 1) HDL levels, 2) LDL levels, and 3) HDL/LDL ratios is realized with the calcium citrate supplementation. The curriculum vitae of declarant/inventor Dr. Ian Reid is also attached. The data demonstrates that a significant benefit with respect to 1) HDL levels, 2) LDL levels, and 3) HDL/LDL ratios is realized with the calcium citrate supplementation. Thus, this new data, like the originally filed data, shows significant benefits not demonstrated in any of the cited references. In addition, the new data and the accompanying Rule 132 declaration also shows that these benefits are maintained at least up to 4 years. The references cited teach that any such benefit of calcium supplementation is minimal and short-lived; the data herein submitted demonstrates that the benefits of **calcium citrate supplementation** on cholesterol levels are

significant and last up to at least 4 years. Mitchell teaches supplementation with calcium gluconogalactogluconate and calcium glycerophosphate (see page 915 of Mitchell); Nutrition Review teaches supplementation with either calcium carbonate and calcium gluconate (see page 299 of Nutrition Review). The benefits of calcium citrate supplementation of the present invention are clearly unexpected in view of the teachings of the cited prior art. The benefits demonstrated, both in this new data as well as in the original application, render the pending claims non-obvious under § 103(a) and patentable over the cited references. Accordingly, applicants respectfully request that the examiner withdraw the pending rejection under § 103(a), and to allow the pending claims.

*2. Interview Summary for Interview of July 25, 2005*

A telephone interview between the applicant's attorney and the examiner was held on July 25, 2005. The outstanding rejection under § 103(a) was discussed. The applicants restated a number of arguments that they have maintained throughout the prosecution of this application. Notably, the applicants argued that the benefits of calcium supplementation described in the instant application is not rendered obvious by any combination of Pak, Nutrition Review or Mitchell. Pak is not concerned with cholesterol, HDL, or LDL levels; Nutrition Review teaches that any benefit on cholesterol levels by calcium supplementation is minor and short-lived (only up to about 4 weeks); Mitchell teaches that cholesterol and triglyceride levels showed little change from the basal levels during the calcium supplementation period. At the suggestion of the examiner during the telephone interview of July 25, 2005, to add further support for these arguments, the applicants herein submit a Rule 132 declaration of inventor Dr. Ian Reid, along with data which demonstrates that a significant benefit with respect to 1) HDL levels, 2) LDL levels, and 3) HDL/LDL ratios is realized with the calcium citrate supplementation. These benefits are clearly unexpected in view of the teachings of the cited prior art. The curriculum vitae of declarant/inventor Dr. Ian Reid is also attached. Applicants assert that this data and the Rule 132 declaration makes clear that the cited prior art, either alone or in combination, does not render the instant claims obvious under §103(a).

**d.) Conclusions**

Applicants herein file an RCE under 37 CFR 1.114, along with a response to the outstanding rejection, including a Rule 132 declaration of inventor Dr. Ian Reid, which includes a curriculum vitae of Dr. Reid and additional data in support of the pending claims. In this reply to the outstanding rejection, applicants also include a formal interview summary as required by the examiner in the office action of August 9, 2005. In light of the Applicants' argument, Applicants respectfully request withdrawal of the outstanding rejections and allowance of the pending claims. If any issues remain outstanding, please contact the undersigned for resolution of the same.

Applicants include the fee for an RCE and the fee for a one-month extension of time. Applicants believe that no other fees are due. However, if applicants are in error and any fees are owing, the Commissioner may charge Deposit Account No. 06-2375, under Order No. P02194US0/10104570, from which the undersigned is authorized to draw.

Respectfully submitted,

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